

REMARKS

The claims in the application are 17-22, corresponding to Claims 1-4, 7 and 13, respectively. The non-elected claims have been deleted without disclaimer of or prejudice to the subject matter deleted therein. No new matter has been added.

The changes made to Claim 17 compared to Claim 1 are the following. The proviso: "except that when X is N, R² together with R³ cannot form =O;" has been added to avoid claiming a compound within the cited Ali reference. The ring c-2 and c-4 have been deleted; this is supported by the specification at p. 14, lines 1-4. The proviso at the end has been deleted as redundant due to the deletion of rings c-2 and c-4.

The double patenting rejection over USSN 10/596,086 is noted as being provisional. The Examiner's attention is directed to two other copending applications, USSN 10/596,083 and USSN 10/595,882. Neither of these claims the same invention as the current application.

The Examiner rejected Claim 3 under 35 USC112, second paragraph as indefinite. This rejection is moot by virtue of the changed language in Claim 17 and Claim 19. The objection to Claim 4, now Claim 20 is also mooted by the correction to the latter.

The Examiner has rejected the claims over the Pailer reference in view of WO/043950. This rejection is incorrect and should be reconsidered and withdrawn. While Pailer and Applicant's claims do have some common structural elements, the Examiner correctly points out that both the variables R1 and the hetero- substituted methylene moiety are differences. In fact, these differences are significant and obviousness is not a permissible inference. Pailer is not simply a positional isomer of Applicants' compounds. Pailer does not suggest any substitution of anything at all on the -CH₂ linking group- the Examiner has found the secondary reference showing hetero rings, but there is no relevance to either the Pailer reference or Applicants' application. There are many "various 5-membered heterocycles" in many references. There is no reason that these references provide motivation to introduce these rings into the Pailer molecule, let alone

render the instant application obvious. The only connection between the two references is Applicants' own invention, and the use of the application to link the references is inappropriate.

5 The Examiner has also rejected the Claim 13, corresponding to Claim 22. The proviso added to Claim 17, deleting the compound from within the scope of this claim, avoids the overlap. Reconsideration and withdrawal of the rejection is respectfully requested.

10 The Examiner's attention is directed to the reference cited by Applicants in the IDS filed in 2006, to EP 0371 564. The deletion of ring c-2 avoids any overlap with this reference, and consequently the proviso at the end of Claim 1 is not necessary in claim 17. The instant is also unobvious over the EP reference.

15 The compounds of the present invention and those of EP 0371 564 contain a phenyl fused with a nitrogen-containing heterocyclic ketone, which is linked to a second phenyl group by means of a spacer.

20 The distinguishing feature between the present compounds of formula (I) and the compounds of EP 0371 564 is the particular kind of spacer, namely
- a bridging group consisting of at least one carbon atom which is substituted on the carbon atom adjacent to the second phenyl group with R^2 and R^3 substituents of which R^3 is different from the heterocyclic ring system disclosed in EP 0371 564. The EP 0371 564 compounds are characterised by an imidazolyl or triazolyl group linked via a
25 nitrogen atom to the carbon spacer between the phenyl fused with a nitrogen-containing heterocyclic ketone and the second phenyl. This is an essential feature of the compounds of EP 0371 564. EP 0371 564 does not teach nor suggest any freedom for modification of this feature.

30 When assessing inventive step, the question to be asked is not whether the skilled man could explore the modification, but rather whether he would explore a certain modification. As stated above, EP 0371 564 limits the heterocycle concerned to imidazolyl or triazolyl linked via a nitrogen atom to the carbon atom of the spacer. Based on this disclosure, the skilled person would not be motivated to explore other
35 heterocycles in said position since there is no disclosure in EP 0371 564 towards other

heterocycles. In order for the skilled man to explore a modification, he needs to have an incentive, a driving force, but this is not provided in EP 0371 564. So based on the teaching of EP 0371 564, the skilled man would not be motivated to explore modifications in the heterocycle at said position. Furthermore, the skilled man also
5 needs to have a reasonable expectation of success. Since EP 0371 564 does not teach any freedom towards other heterocycles at said position of the compound, there is no reasonable expectation for the skilled man that if he explores other heterocycles at said position, that this would still result in active compounds.

10 Furthermore, the skilled man would certainly not be motivated to explore substituents in said position other than heterocycles and the skilled man would also not be motivated to explore compounds having one or more additional carbon atoms in the spacer between the phenyl fused with a nitrogen-containing heterocyclic ketone and the carbon atom carrying the Y and imidazole/triazole heterocycle because there is no
15 teaching, no disclosure whatsoever on such a modification in EP 0371 564.

In addition, the compounds of EP 0371 564 are described as suppressing the plasma elimination of retinoic acids and inhibiting the formation of androgens from progestrines or inhibiting the action of the enzyme complex aromatase. In view of this
20 activity, the compounds of EP 0371 564 can be used in the treatment of disorders which are characterized by an increased proliferation or abnormal differentiation of epithelial cells, such as carcinoma's and disorders of keratinisation, and they can be used in the treatment of estrogen or androgen dependent disorders such as e.g. breast and prostatic cancer.

25 With the present invention, it was now found that the present compounds exhibit poly(ADP-ribose)polymerase inhibiting activity. Because of this activity, the compounds can be used therapeutically in a variety of disorders. In this respect, we wish to refer to the teaching on pages 1-5 and pages 27-31. The compounds of the
30 instant application exhibit another pharmacological profile than that described for the compounds of EP 0371 564. For instance, the present compounds ameliorate neural or cardiovascular tissue damage, they can radiosensitize or chemosensitize cells, they can spare the cells from energy loss, they are useful for the treatment of e.g. leukemia and lymphoma's.

35 This pharmacological profile of the present compounds, which is clearly different from the profile of the compounds of EP 0371 564, could not have been deduced from

the teaching of the claims of this case. There is no indication or suggestion towards PARP inhibiting activity in EP 0371 564.

- 5 The application is in condition for allowance. Favorable action on the merits is respectfully requested. Applicant respectfully requests a timely Notice of Allowance.

Respectfully submitted,

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